Rituximab in Primary Central Nervous system Lymphoma.
A randomized HOVON / ALLG intergroup study

Published: 20-10-2009
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Primary objectiveTo assess the effect of the addition of rituximab in a standard chemotherapy regime on EFS in newly diagnosed PCNSL.Secondary objectiveTo evaluate the effect of the addition of rituximab to a standard chemotherapy regimen with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas non-Hodgkin's B-cell
Study type	Interventional

Summary

ID

NL-OMON43562

Source
ToetsingOnline

Brief title
HOVON 105 PCNSL

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
Primary Central Nervous system Lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: HOVON

Source(s) of monetary or material Support: KWF Kankerbestrijding;Stichting HOVON,Roche Nederland BV

Intervention

Keyword: Chemotherapy, Event Free Survival, PCNSL, Rituximab

Outcome measures

Primary outcome

- Event free survival

Secondary outcome

- Response rates after (R-) MBVP, after cytarabine and after completion of

radiotherapy

- Toxicity

- Overall survival

- Cognitive function and quality of life after treatment

Study description

Background summary

For patients with primary central nervous system lymphoma (PCNSL) in a reasonable or good clinical condition, standard treatment is chemotherapy with high dose methotrexate (HD-MTX) frequently combined with other chemotherapy agents. In patients up to 60 years of age this is generally followed by whole brain radiotherapy. In the Netherlands the MBVP (HD-MTX, BCNU, teniposide, prednison) schedule is customary in most centres. With this treatment approximately 30% of patients achieve long-term remission and possibly cure. A recent randomized study has shown improved survival after the addition of cytarabine to HD-MTX treatment. Besides this, the incorporation of intravenous rituximab into the treatment of systemic lymphoma has resulted in a 15-20% improvement in survival. It is unknown whether rituximab is effective in PCNSL: the protective blood-brain-barrier may prevent rituximab from reaching the brain tumor. The effect of rituximab on PCNSL will be investigated in this study.

Study objective

Primary objective
To assess the effect of the addition of rituximab in a standard chemotherapy regime on EFS in newly diagnosed PCNSL.

Secondary objective
To evaluate the effect of the addition of rituximab to a standard chemotherapy regimen with respect to toxicity

Study design

a prospective randomized multicentre (intergroup) phase III study.

Intervention

All patients will be treated with MBVP chemotherapy followed by cytarabine and, in patients up to 60 years of age, whole brain radiotherapy. In addition, patients randomized to the investigational arm will be treated with intravenous rituximab.

Study burden and risks

Intensive treatment with chemotherapy requires several hospital admissions. This is necessary to safely administer the chemotherapy, to observe the patient and to monitor side effects. This is common for most intensive treatments in hematology. Methotrexate can induce renal insufficiency and all chemotherapy can induce neutropenia and complications of infectious nature

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients with a histologically confirmed diagnosis of CD20 positive DLBCL based upon a representative histology specimen of brain biopsy according to the WHO classification
OR
Patients with a diagnosis of PCNSL based on MRI evidence of brain parenchymal lesion showing homogeneous contrast enhancement suspect for lymphoma
AND Unequivocal morphological and/or immunophenotypical evidence of CSF
CD20 + large cell lymphoma AND/OR Unequivocal morphological and/or immunophenotypical evidence of CD20 + large cell lymphoma in vitreous fluid
OR
Patients with unequivocal morphological and/or immunophenotypical evidence of CD20 + large cell lymphoma in vitreous fluid AND CSF but without a brain parenchymal lesion
-Age 18-70 years inclusive
-Performance status with or without administration of steroids WHO 0 * 3
-Written informed consent

Exclusion criteria

-Evidence of systemic lymphoma
-History of intolerance of exogenous protein administration
-Severe cardiac dysfunction (NYHA classification III-IV, or LVEF < 45%) Congestive heart failure or symptomatic coronary artery disease or cardiac arythmias not well controlled with medication
-Severe pulmonary dysfunction (vital capacity or diffusion capacity < 50% of predicted value)
-Significant hepatic dysfunction (bilirubin or transaminase * 2.5 x upper normal limit).
-Significant renal dysfunction (serum creatinine *150 umol/l or clearance < 60 ml/min
-Presence of *third space fluid*, such as pleural effusion or ascites
-Prior cranial radiotherapy

-Active uncontrolled infection
-HIV-positivity
-(EBV positive) post-transplant lymphoproliferative disorder
-Untreated hepatitis B infection (inclusion is possible if adequate antiviral medication e.g. lamivudine or alternative is started)
-Positive pregnancy test in women of reproductive potential
-Lactating women
-Unable or unwilling to use adequate contraceptive methods (all men, pre-menopausal women)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-07-2010
Enrollment:	130
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Mabthera
Generic name:	Rituximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	20-10-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-07-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-04-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-05-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-03-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-05-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-05-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	20-02-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-02-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-02-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	29-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-04-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-014722-42-NL
CCMO	NL29231.078.09